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Response to advanced notice of proposed rulemaking: Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding is Sought and Responsible Prospective Contractors [Docket No. NIH–2008–0002.]

Dear Mr. Moore,

The Pew Prescription Project is an initiative of The Pew Charitable Trusts to promote consumer safety through reforms in the approval, manufacture and marketing of prescription drugs, as well as through initiatives to encourage evidence-based prescribing. The Pew Prescription Project conducts rigorous nonpartisan research related to federal oversight of drug safety to better illuminate problems and potential solutions. The Project also promotes public and private-sector policy solutions that reduce conflicts of interest in the medical profession to maximize benefits and minimize risks to patients.

Community Catalyst is a national non-profit advocacy organization working to build the consumer and community leadership that is required to transform the American health system. Its staff of experienced policy analysts, attorneys, community organizers, and communications specialists has worked with organizations in over 40 states, and has helped these organizations achieve wide-reaching reforms in many areas including Medicaid policy, prescription drug prices, and diversity in the health care workforce.

The Pew Prescription Project and Community Catalyst (RxP/CC) strongly support the principles NIH has presented as a basis for revised guidelines on investigator disclosure and management of conflicts, and we commend the Institute's initiative to reexamine the controls in place to ensure objective and responsible research.

Managing the real and perceived conflicts of interest of biomedical researchers, as well as other medical professionals, has become increasingly critical each year since the 1980 passage of Bayh-Dole Act, which encouraged collaboration between researchers and the pharmaceutical and medical device industries. Academic-industry collaboration is necessary and beneficial, but creates conflicts of interest that must be managed. PHS regulations 42 CFR Part 50 Subpart F and 45 CFR Part 94 were instituted in 1995 in response to concerns that financial relationships with industry may insert bias into federally-funded studies. Since that time compliance with these and other regulations, and the quality of disclosure, reporting, and management of conflicts of interest has been called into question.

Recent examples of inconsistent and incomplete reporting of financial conflicts related to public health service funding validate NIH's efforts to reexamine current regulations. For instance, investigations by Sen. Charles Grassley (R-IA) in 2008 revealed that three child psychiatrists at Harvard failed to report $3.2 million in income received directly from drug companies or through third-parties. In some cases, the financial relationships were with companies whose products were being tested in NIH-sponsored clinical trials run by these same researchers. Harvard rules, in existence at the time of these incomplete disclosures, prevent a faculty member from researching a company's drug if he or she receives more than $20,000 a year in consulting fees or honoraria from that company.

In another high-profile incident last year, Sen. Grassley's investigations revealed that Dr. Charles Nemeroff, the chair of the Emory University psychiatry department, vastly underreported his earnings from drug companies in voluntary disclosure forms to the University, accepting nearly $1 million from GlaxoSmithKline between 2000-2006, but only reporting $35,000 in earnings over that same time period. Those payments were not, in turn, reported to the NIH. Dr. Nemeroff was concurrently serving as principal investigator on a trial of a GlaxoSmithKline drug supported by a $3.9 million grant from the National Institute of Mental Health, and the scope of GSK's actual payments to him would have required Emory to report them to NIH as a Financial Conflict-of-Interest (FCOI). Lack of sufficient enforcement of institutional disclosure requirements allowed, in part, these troubling reporting omissions to go unnoticed by the system.

These examples, along with others that have surfaced in Congressional investigations over the last two years, demonstrate that a discretionary reporting system, when unchecked, can miss relevant financial relationships, and, in the worst of cases, can be abused. Considering these events, RxP/CC offers the following responses to specific questions raised by NIH.

I(b) Should Investigators be required to disclose to their Institutions all Significant Financial Interests that are related to their Institutional responsibilities? Would this expanded disclosure allow the Institution to better determine which of these Significant Financial Interests constitute a FCOI?

Current NIH regulations require investigators to selectively disclose Significant Financial Interests (SFIs) to their institution by making their own determination about whether these relationships "might reasonably appear to be affected" by federally-funded research. The current system relies on a researcher's self-assessment of the relevance of a financial relationship. This assessment should be made by the institution. In addition, the varied individual interpretations of these disclosure criteria will almost necessarily yield inconsistent data, and limiting Investigator disclosures to transfers of value above $10,000 and 5% equity interest per year as in the current standard can unintentionally prevent disclosure of relationships that the Institution may determine to be conflicts. NIH relies on institutions to inform them of any and all potential conflicts among researchers in order to ensure federally funded studies are not subject to bias; NIH thus has a logical interest in institutional abilities to identify and report those conflicts.

RxP/CC recommends that all biomedical researchers (as well as all other institutional faculty, staff, and administrators) disclose all financial relationships related to their professional responsibilities to their institutions, regardless of amount. This will enable institutions to most effectively identify financial conflicts, and will further help remove the question of conflicts where they do not exist.

Such robust policies are already in place at many institutions, having become increasingly prevalent over the past few years due to the support of comprehensive disclosure by national organizations such as the Institute of Medicine (IOM)[1], the Association of American Medical Colleges (AAMC), the Association of American Universities(AAU)[2], and the American Medical Student Association(AMSA)[3], as well as pressures from congress and the public.

II(a) Should the current exemptions [for Significant Financial Interests] be maintained?

If so, are the current de minimis thresholds ($10,000 and 5 percent ownership interest in any single entity) reasonable? If not, how should the de minimis thresholds be changed? Should these thresholds be the same for all types of research?

If not, which exemptions should be reconsidered, and why?

Current policy requires that Investigators disclose only Significant Financial Interests (SFI) to Institutions, and therefore only financial conflicts meeting the SFI definition may eventually be reported to NIH. As previously discussed, RxP/CC recommends all financial relationships related to professional responsibilities, regardless of value or relation to research, should be reported by Investigators to Institutions. Institutions should assess the potential significance of any financial relationship, regardless of value (excluding ownership or income derived from publicly traded security and mutual funds).

For reporting purposes, the current thresholds in the definition of SFI (i.e. less than $10,000 and less than 5 percent ownership interest) should be lowered.

III(c) Should Investigators who are involved in participant selection, the informed consent process, and clinical management of a trial, be prohibited from having a Significant Financial Interest in any company whose interests could be affected by their research or clinical trial? If so, what special circumstances would justify waiving this condition, if any?

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[1] Field, Marilyn J. and Lo, Bernard, Eds. "Conflict of Interest in Medical Research, Education, and Practice" Committee on Conflict of Interest in Medical Research, Education and Practice, Board on Health Sciences Policy, Institute of Medicine. 2009

[2] Association of American Medical Colleges & Association of American Universities "Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research. A Report of the AAMC-AAU Advisory Committee on Financial Conflicts of Interest in Human Subjects Research" February 2008

[3] AMSA PharmFree Scorecard 2009. Methodology (online), http://www.amsascorecard.org/methodology, Reston, VA: American Medical Student Association July 6, 2009

Multiple entities have identified the increased scrutiny necessary for financial interests related to research with human participants. IOM, AAMC and AAU have all urged institutions to generally prohibit individuals from conducting human subjects research when they have a significant financial relationships related to the research, and only allow this when the researcher's participation is judged critical for the safety and validity of the research.

RxP/CC recommends that NIH require institutions to have such policies in place, and that any exceptions to such policies should be reported to NIH and to the public, along with an explanation of the exception and a summary of the plan to manage the conflict.

IV(a) Should the regulations enhance existing enforcement options in the event of noncompliance?

RxP/CC believes that the increased reporting requirements discussed in these comments would better equip NIH to manage conflicts of interest and respond to NIH inquiries about specific individuals and grants. Broadening the scope of conflicts of interest reported under the proposed requirements would increase the Institutes' ability to actively monitor them.

IV(c) Should independent confirmation of an Institution's compliance with the regulation be required? If so, what should this confirmation look like (e.g., accreditation by an outside body, an independent audit)?

A formal and systematic cross-check is critical to the success of conflict-of-interest regulation and reporting standards. Proposed federal legislation, such as the Physician Payments Sunshine Act (S.301), introduced by Sens Grassley and Kohl and counterpart legislation included in the House Tri-Committee health reform proposal, offers a rational, reliable, and independent set of data that may be used by Institutions or NIH to validate compliance. The Sunshine Act would create a national publicly-searchable online database into which all prescription drug and medical device companies would be required to report payments to prescribers and covered recipients. In the House Tri-Committee health reform proposal, biomedical researchers are included among covered recipients.

V(a) Should Institutions be required to submit to the PHS funding component additional information on any identified conflict? If they should not be required to submit additional information for all identified conflicts, should they be required to submit additional information for identified conflicts involving certain types of research? If so, for which types of research? What kind of information would provide valuable data to the PHS funding component in evaluating these reports and the potential risk of bias in conduct of research?

Currently, institutions report to NIH the existence of identified Financial Conflicts of Interest and an assurance that these conflicts are being managed by the Institution. As stated earlier, reporting of additional information to NIH will facilitate the awarding body's oversight and enforcement of institutional compliance with 42 CFR Part 50 Subpart F and 45 CFR Part 94, and will help ensure

institutional compliance with NIH regulations. As such the provision of additional information should not be restricted to any specific type of research.

As discussed above, RxP/CC believes that the Physician Payments Sunshine Act will serve as an important tool for Institutions and NIH to cross-check compliance by both Investigators and Institutions with NIH regulation. Therefore RxP/CC strongly recommends that the information reported to NIH for FCOIs align with the reporting requirements outlined in the Sunshine Act legislation. The ability to easily and thoroughly cross-reference disclosures will be an essential for the functioning of the Sunshine Act as a mechanism to validate compliance.

The Physician Payment Sunshine Act will allow for immediate comparison of most financial disclosures; however, payments related to clinical research under S.301would not be disclosed for several years after the fact. NIH and other federal agencies should have access to this information without delay.

RxP/CC urges NIH to require the information reported for FCOIs include:

- Investigator name
- Award number
- Amount of financial interest
- Form of financial interest (cash, in-kind, stock, stock option, dividend, public or private equity)
- Date(s) of financial interest
- Name of the related drug, device or supply, where available
- Specific category(ies) of financial relationships currently included in the Physician Payments Sunshine Act. These include: Gifts; food; entertainment; travel or trip; honoraria; consulting fees; research funding or grant; education or conference funding; ownership or investment interest.

RxP/CC are grateful for the opportunity to comment on this advanced notice of proposed rulemaking by NIH. Increased transparency of financial conflicts of interest between medical professionals and industry has been called for by academic medical centers, professional medical organizations, congress, and consumer groups alike. Ensuring the relationships between federally-funded investigators and industry are appropriate and transparent is a critical task that will serve academia, industry, and most importantly will protect the public health.

Sincerely,

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